



## ORAL PRESENTATION

## Open Access

# Monophosphoryl Lipid A as an adjuvant for immune therapy? A detailed *in vitro* comparison to LPS

Stefan Schülke<sup>1\*</sup>, Lothar Vogel<sup>2</sup>, Adam Flaczyk<sup>2</sup>, Sonja Wolfheimer<sup>2</sup>, Stefan Vieths<sup>2</sup>, Stefan Scheurer<sup>2</sup>*From* 5th International Symposium on Molecular Allergology (ISMA 2013)  
Vienna, Austria. 6-7 December 2013

Monophosphoryl lipid A (MPL) is a non-toxic TLR4 ligand, derived from *Salmonella minnesota* R595 (Re) lipopolysaccharide (LPS) by chemical modification. It is clinically used as an adjuvant for cancer treatment (Fendrix<sup>®</sup>, Ceravix<sup>®</sup>) and allergen specific immunotherapy (Pollinex<sup>®</sup> Quattro, ORALVAC<sup>®</sup>). Nevertheless, reports on the mechanism of adjuvant activity are limited. The aim of this study was to compare the immune modulating capacities of MPL and LPS *in vitro*.

In both human and murine lung epithelial cell lines (LA-4, A549) LPS induced a higher CCL2 secretion than MPL. In murine BM-derived myeloid dendritic cells (mDC), LPS as well as MPL stimulation resulted in the same pattern of cytokine secretion (IL-1 $\beta$ , IL-6, IL-10 and TNF- $\alpha$ ). At high concentrations of MPL, IL-1 $\beta$  secretion was 4-fold higher compared to LPS, whereas LPS stimulation resulted in higher secretion of IL-6, IL-10 and TNF- $\alpha$ , respectively. Moreover, mDC stimulation with both adjuvants resulted in a pronounced cell activation pattern characterized by CD40 and CD69 upregulation, at which LPS proved to be more potent than MPL (thresholds for mDC activation: MPL: 100 ng/ml, LPS: 1 ng/ml). In MyD88<sup>-/-</sup> and Trif<sup>-/-</sup> mDC, MPL-induced cytokine secretion was absent in MyD88- but only reduced in Trif-deficient mDC. LPS induced cytokine secretion was mostly unchanged in Trif<sup>-/-</sup> mDC. Furthermore, the co-administration of MPL and Ova resulted in enhanced IFN- $\gamma$  and IL-5 secretion from OVA-specific DO11.10 CD4<sup>+</sup> T cells co-cultured with BALB/c mDC which was not observed for LPS controls. In line with this result, stimulation with a covalent fusion protein of MPL and Ova (MPL:Ova) resulted in enhanced cytokine secretion from both mDC

(IL-1 $\beta$ , IL-6, TNF, IL-10, IL-12) and CD4 T cells (IL-5, IL-13, IL-2, IFN- $\gamma$ , IL-17) compared to equimolar concentrations of MPL and Ova provided individually or as a mixture. Interestingly, Ova induced IL-9 secretion from CD4<sup>+</sup> T cells was dose-dependently repressed when fused to MPL.

In summary, using *in vitro* assay systems we observed similar but attenuated immune responses induced by MPL in comparison to LPS. MPL applied together with allergen (either mixed or covalently fused) on CD4<sup>+</sup> T cells boosted allergen-specific TH1-, TH2-, and TH17-adaptive responses. Although considered safe in humans, further studies should critically assess the adjuvant capacity of MPL in order to evaluate potential non-desired immunological effects.

**Authors' details**<sup>1</sup>Paul-Ehrlich-Institut, Paul-Ehrlich Straße 51-59, Langen (Hessen), 63225, Germany. <sup>2</sup>Paul-Ehrlich Institut, Division of Allergology, Langen, Germany.

Published: 17 March 2014

doi:10.1186/2045-7022-4-S2-O21

**Cite this article as:** Schülke et al.: Monophosphoryl Lipid A as an adjuvant for immune therapy? A detailed *in vitro* comparison to LPS. *Clinical and Translational Allergy* 2014 **4**(Suppl 2):O21.<sup>1</sup>Paul-Ehrlich-Institut, Paul-Ehrlich Straße 51-59, Langen (Hessen), 63225, Germany

Full list of author information is available at the end of the article